

January 15, 1999

This document was submitted to EPA by a registrant in connection with EPA's evaluation of this chemical, and it is presented here exactly as submitted.



DuPont Agricultural Products

December 14, 1998

Dr. John Newland
Chlorethoxyfos Review Manager, Branch 1
Reregistration Review and Registration Division (7508C)
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, Virginia 22202

Subject: *DuPont Response to Preliminary Risk Assessment for Chlorethoxyfos, the Active Ingredient of Fortress® 5G in the SmartBox™, Fortress® 2.5G and Fortress® Technical [EPA Reg. Nos. 352-552, 352-579, 352-553]*

Refs: *Letter received Nov. 12, 1996, Dr. John Newland, EPA, to Dr. Linda Carter, DuPont Agricultural Products, transmitting Preliminary Human Health Risk Assessment for Chlorethoxyfos, including: "Chlorethoxyfos- Short Format HED Chapter of RED, Chemical Number 129006 and supporting documents". Revised Short Format HED Chapter of RED and attachment received Nov. 24, 1998.*

Dear Dr. Newland:

DuPont received your correspondence on November 12, 1998 requesting initial review of the preliminary human health risk assessment for chlorethoxyfos, the active ingredient in Fortress® Brand Granular Insecticides. We are providing our comments via this letter and its attachments. We thank you for taking the extra effort to ensure we had the most recent documents for drinking water risk assessment (received November 24, 1998).

While we have closely examined the scientific basis and methods for each area of hazard identification and risk assessment, we will focus comments on potential mistakes, such as mathematical, computational, typographic or other similar errors, including those that differ from recent EPA risk assessments.

As noted below and in Attachment I, certain corrections should be made in Tables 1, 2, 6 (surface water modeling results), Tables 6 and 7 (occupational exposure) and the resultant text of hazard and exposure assessment. References pertaining to these corrections are contained in Attachment II. All references are EPA documents, which substantiate the source of the corrected information. Attachment III provides a copy of the Agency's July 1998 occupational risk assessment conducted for Fortress® 5G in the SmartBox™.

We urge the Agency to correct the following errors (types noted above) in the Revised Short Format HED Chapter of the RED (November 24, 1998), before placing this document in the public docket.

I. Hazard Assessment

A. Hazard Identification

Changes to Table 1 Toxicity Profile of Chlorethoxyfos: (References for changes noted in Attachment II)

- 21-day dermal rat toxicity study: (See Reference 1)
 - Note the NOEL and LOEL in Table 1 are for Fortress® 5G, since this study was conducted with this end use product (as required by conditional registration).

Therefore,

- Change the NOEL and LOEL to reflect exposure to chlorethoxyfos (5% of 5G granule).

NOEL = 1.25 mg/kg/day (ChE inhibition)

LOEL = 3.75 mg/kg/day (ChE inhibition)

- Reproductive Toxicity: (References 2 and 3)
 - Correct decimal point error in Reproductive Toxicity NOEL and LOEL for Offspring.

NOEL = 0.607 mg/kg/day (HDT) (not 0.0607)

LOEL = >0.607 (greater than highest dose tested) (Not >0.0607)

We concur with the EPA that DuPont has provided a complete toxicology database to enable the Agency to make appropriate scientific-based toxicology determinations, such as endpoint selection and risk assessment. We do note that review of the following studies, required by conditional registration to complement the HED database, is still pending:

- | | | |
|---|---------------------------------|---|
| • Acute oral neurotoxicity study (Fortress® Technical) | submitted March 1997 (44234601) | Confirms results from previous study. |
| • Repeated dose inhalation toxicity study (Fortress® Technical) | submitted April 1997 (44382101) | Applicable to refining worker risk assessment |
| • 28-day hen delayed neurotoxicity study | October 1997 (44414001) | Confirms no evidence of OPIDN in hens. |

We appreciate EPA's extension of the conditional registration of chlorethoxyfos containing products until September 2001 to permit review of these studies.

B. Dose Response Assessment (See Attachment II for references)

1. Determination of Susceptibility

For accuracy, the Agency should make the following change to Table 2:
Toxicology Endpoints Selected for Risk Assessments:

Short term and Intermediate term Dermal Exposure

- 21-Day dermal rat toxicity study: (Reference 1)
 - Note that the NOEL in Table 2 is for Fortress® 5G Insecticide, since this study was conducted with this end use product (as required by conditional registration).

Therefore,

- Change the NOEL to reflect exposure to chlorethoxyfos (5% of 5G granule).

NOEL = 1.25 mg/kg/day (ChE inhibition)

We agree with the Agency that the completeness of our chlorethoxyfos database, along with the weight of evidence, demonstrates that there is no increased susceptibility of offspring to chlorethoxyfos (References 1-3). This weight of evidence supports the use of an uncertainty factor of 100.

II. Exposure Assessment

A. Registered Uses: No changes.

We believe the Agency has adequately characterized the uses and other planting use conditions accurately. The label states an application rate in terms of oz. per 1000 row feet. The RED document states rate in pounds/acre.

B. Dietary Exposure: No changes.

As the Agency has noted, the metabolism and nature of residue in corn and animals is adequately understood and residues in corn commodities are less than 0.01 ppm for all corn commodities (non-detectable).

1. and 2.: Acute and Chronic Dietary Exposure (Food):
No changes to Tables 3 and 4.

We agree with EPA that Tier I worst case dietary (food) exposure assessment for chlorethoxyfos could be refined and would become even less than denoted in Tables 3 and 4. We agree with the Agency that even worst case Tier I analysis, utilizes only a very small percentage of the acute (U.S. Population: 1% and Infants <1 yr. old: 3%) and chronic (US Population: 1% and Infants <1 year old, 2%) reference dose.

C. Drinking Water Exposure

1. Surface Water

We agree with the Agency that drinking water exposure clearly does not exceed HED's level of concern. We note, however, that the exposure calculations for surface water do not reflect the estimated environmental concentrations (EECs) for chlorethoxyfos in water that the Agency accepted in 1994. Although all of the underlying studies and data are the same as used in 1994, the results of the 1998 estimation indicate that different input parameters were selected for modeling. We request a copy of the details used in EPA's most recent calculations.

For in-furrow application, the acute and chronic EECs should be 0.006 and 0.003 parts per billion, respectively. For T-Band application, the acute and chronic EECs should be 0.013 and 0.006 parts per billion, respectively. A difference in half-life may provide rationale for the differences. In 1994, the Agency accepted a half-life of 7 days. (Reference 4) EPA's most recent calculations (11/23/98) use a soil half -life of 20-23 days.

We also urge the Agency to use consistent units in reporting the DWLOCs (U.S. Population is 21 parts per billion and children 1-6 is 6 parts per billion) and exposure for chlorethoxyfos (parts per billion).

2. Groundwater:

For consistency, we recommend using 0.002 parts per billion instead of 2 ppt.

D. Occupational Exposure: (See attachment II for References to Corrections.)
Table 6 Occupational Handler Exposure Estimate and Risk Assessment

1. Summary Dermal Exposure changes (References 4 and 5):

- Correct loader dermal exposure (NOEL = 25 mg/k/d): Correct value is 300,000 (not 30, 000). However, the Margins of Exposure (handlers, applicators) should be corrected to reflect the new short and intermediate term dermal NOEL (chlorethoxyfos = 1.25 mg/kg/d) (See page 5 of this letter for corrections).

Table 6: Occupational Handler Exposure Estimate and Risk Assessment Summary
Chlorethoxyfos [DuPont Fortress® 5G in SmartBox]

Application Scenario	Dermal			Inhalation						Combined MOE
	(With Minimum PPE)*			(Attachment II, Reference 4)						
	UE ^b (mg/lb/a.L)	ADD ^c (mg/kg/d)	MOE ^e (NOEL = 1.25 mg/kg/d)	Exposure Concentration (ng a.L/L)	Activity Factor (l/hr)	Exposure Duration (hrs/d)	Exposure (mg a.L/d)	ADD ^d (mg/kg/d)	MOE ^e (NOEL = 0.06 mg/kg)	
SmartBox™ using a closed-cab tractor and planter										MOE Total ^f
Loader	0.0002	0.000084	14,800	0.22	1000	0.25 hr	0.000055	0.00000079	75,950	12,390
Applicator	0.0008	0.00034	3,675	0.14	500	7.75 hr	0.00055	0.00000079	7,575	2,475
Combined	0.001	0.00042	2,950	-	-	-	-	0.00000087	6,950	2,070

- The minimum PPE is long sleeve shirt, long pants, shoes, socks and waterproof gloves
- UE = Unit Exposure is the amount of exposure measured in study in terms of mg a.i./lb a.i. handled
- ADD (mg/kg/d) = unit exposure (UE) from studies in mg/lb a.i. handled * 29.25 lb a.i./d/70 kg wt
- Inhalation ADD (mg/kg/day) = Inhalation Exposure concentration from studies in ng a.i./l * Activity Factor in l/hr from EPA Exposure Factors Handbook (1997) for appropriate activity * Exposure Duration in hrs/d for that activity during the work day. Combined Inhalation ADD is the sum of Loader and Applicator Inhalation ADD's
- MOE = NOEL/ADD
- Combined MOE is based upon formula: the inverse of the sum of the inverses of the dermal and inhalation MOEs. See reference 5.

Note: NOEL Dermal = 1.25 mg/kg/d
Exposure Inhalation and Dermal based on July 1998 assessment by Jack Arthur, HED, (Attachment III)

2. Summary of Inhalation Exposure Changes (See Attachment II for corrections)

- Use data from July 1998 exposure assessment. (References 4 and 5)
An assessment of inhalation exposure for Fortress® 5G was conducted in July 1998 (J. Arthur, HED, Reference 4), after review of the Applicator Exposure Study with Fortress® 5G in the SmartBox™. This assessment uses the same endpoint as the one noted in the chlorethoxyfos RED but uses HED's recommended methodology for inhalation risk assessment as described in the Document "Inhalation Risk Assessment and the Combining of Margins of Exposure. (Reference 6)
- Margin of Exposure Calculations. (Reference 4)
Margins of exposure should be recalculated, using the July 1998 exposure assessment and the revised dermal NOEL, since that document followed the 1997 HED guidelines. (Attachment III)
- The data for Fortress® 2.5 G should be updated in a similar manner.

We appreciate the opportunity to comment on the revised preliminary risk assessment of chlorethoxyfos and the revised Short Format HED Chapter of the Reregistration Eligibility Document before these documents are placed in the public docket. Such a process is important to ensure that the most current and correct information is in the docket.

We trust you will give serious consideration to making our recommended corrections and look forward to reviewing the version of the preliminary risk assessment of chlorethoxyfos that is placed in the docket.

Again, thank you for ensuring we had the most current exposure assessments and answering questions I had about procedures to respond to the risk assessment document.

Best wishes with your new assignment.

Please call if you have any questions (302-992-6263).

Sincerely,



Linda G. Carter, Ph.D.
U.S. Product Registration Manager

Attachment II

List of References

1. "Chlorethoxyfos-Re-Evaluation of Toxicology Endpoint Selection," Hazard Identification Assessment Review Committee, HED, October 19, 1998.
2. "Chlorethoxyfos- FQPA Requirement- Report of Hazard Identification and Assessment Review Committee," HED, September 25, 1997.
3. A) "Hazard Assessment of the Organophosphates, Report of the Hazard Identification Assessment Review Committee," HED, July 7, 1998.
B) "FQPA Safety Factor Recommendations for Organophosphates (A combined Report of the Hazard Identification Assessment Review Committee and the FQPA Safety Factor Committee, HED, August 6, 1999.
4. "Environmental Fate and Groundwater Branch Review Action," H. Jacoby, EFED, to Dennis Edwards, RD, July 13, 1995.
5. "Review of Worker Exposure Risk Assessment for Fortress® 5G in the SmartBox™ Closed Handling and Application System" (DP Barcode: D241107):
Chem ID# 129006, EPA Reg No.: 352-552 MRID # 443998-02, July 27, 1998
Jack Arthur, HED, to Beth Edwards, Registration Division
6. "Inhalation Risk Assessments and the Combining of Margins of Exposure,"
J.E. Whelan and H.M. Pettigrew, HED, February 10, 1997.